Introduction

The prognosis of advanced cancer is extremely poor. Thus the future of gastrointestinal (GI) cancer lies in its early detection, best done through screening of the high risk population. The currently recommended gold standard detection tool for GI cancer is white light endoscopy, which has drawbacks including dependency on the operator’s skill. As a result, biopsy sampling is typically random in nature which adds significantly to the procedural cost. Furthermore, sampling errors can lead to an inaccurate diagnosis. Thus, there are unmet needs in terms of realtime diagnosis in order to enable the following strategies:- (i) Diagnose & Leave: this strategy will obviate unnecessary biopsies; (ii) Diagnose & Target: this strategy will facilitate targeted biopsies and improve yield; (iii) Diagnose & Resect: this strategy will aid management decision in terms of the best approach, e.g., ESD for cancer; EMR for dysplasia; (iv) Diagnose & Mark: this strategy will allow the endoscopist to decide on the precise resection margin; and finally, (v) Resect & Discard: this strategy will obviate unnecessary pathology, and save cost.

Several imaging-enhanced technologies allowing negative predictive values ≥90% have emerged in the hope of improving the above diagnostic algorithms. The question is do these technologies provide real-time diagnosis for real-time decisions?

Currently available imaging-enhanced technologies

1. Narrow Band Imaging (NBI)

NBI has been shown to enhance the mucosal surface architecture and vasculature. The downsides include the fact that no agreed consensus exists for mucosal and vascular pattern classifications, as well as limited data comparing inter- and intra-observer variability. A study from US showed that only 25% of community-based gastroenterologists were able to use NBI to assess polyps with ≥90% accuracy.¹ The authors concluded that better results in community practice must be achieved before NBI-based optical biopsy methods can be used routinely to evaluate polyps.
2. Confocal laser endomicroscopy (CLE)

While CLE is able to magnify images 1000x and in doing so, allows the operator to do realtime histological diagnosis of abnormal tissue. However, it requires a long learning curve in order to acquire the skill needed to interpret the images with sufficient accuracy. A previous study from our centre showed significant difference in accuracy between experienced and inexperienced operators in term of image interpretation. Another study corroborated our finding showing wide discrepancy in the interpretation of pCLE findings between endoscopists and pathologist.

3. Optical coherence tomography (OCT)

OCT has the potential to enhance the operator’s morphological understanding of tissue in real time. However, present studies demonstrate variation in both sensitivity and specificity which may be due to the limited scanning depth and subjectivity of operator interpretation.

Realtime decision making

The Preservation and Incorporation of Valuable endoscopic Innovations (PIVI) initiative courtesy of the American Society for Gastrointestinal Endoscopy (ASGE) recommends a need for imaging systems that help to limit the need for biopsy sampling with development of technologies. Thus, to enable the “Diagnose-and-leave” strategy for diminutive polyps, PIVI recommends that endoscopic diagnosis should provide a ≥ 90% negative predictive value for adenomatous histology. For the “Resect-and-discard” strategy for diminutive adenomas, PIVI recommends that endoscopic characterization should provide a ≥ 90% agreement compared with decisions based on pathology assessment. While some of the currently available imaging-enhanced technologies may achieve these threshold values in expert hands, learning curve to achieve accurate optical diagnosis remains a challenge for most endoscopists. A realtime objective diagnostic tool is much needed to achieve the PIVI’s vision.

Objective, real time in-vivo molecular diagnostic system

We have developed the world’s one-of-a-kind In-Vivo Molecular Diagnostic System, which is capable of providing real-time and operator-independent diagnosis of tissues during endoscopic examination. It is based on Raman spectroscopy - a vibrational technique that enables molecular information to be captured when tissue molecules are agitated by a laser beam. The fibre-optic probe delivers a laser beam and captures the molecular ‘fingerprint’ of any tissue it comes into contact with - and the information is analyzed in real-time. Cancerous and precancerous tissues have different molecular ‘fingerprint’ from healthy tissue - so a diagnosis is provided in <1 second. Proof of effectiveness has been demonstrated in close to 1,000 patients with a diagnostic accuracy of >90% for stomach, esophageal and colon cancerous tissues. Its significance lies in the ability of the technology to allow clinical decision on the spot, potentially enabling strategies such as “diagnose & discard”, “diagnose and target”, “diagnose & resect”, “diagnose & mark”, and “resect & discard”, thus saving time, cost, and minimizing complications by obviating unnecessary biopsy, and limiting resection margin.
Conclusion

Despite the gold standard of white light endoscopy, additional platforms such as NBI, CLE, and OCT have emerged to enhance the characterization process during endoscopic examination. They all suffer from the shortcoming of operator variability. A realtime and objective diagnostic tool is much needed to overcome this shortcoming. We believe the Raman spectroscopy based in-vivo molecular diagnostic system has the potential to fill this unmet need. Preliminary results done on gastric, esophageal and colorectal issues from close to 1,000 patients are most encouraging.

References